IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Luc R. Mongeon, Jesus Casas-Bejar, H. Toby Markowitz, Daisy P. Cross, Janelle Blum, Michael Ebert and Timothy G. Laske	Confirmation No.	2842
Serial No.:	10/663,570	Group Art Unit:	3762
Filed:	September 15, 2003	Customer No.:	28863
Examiner:	Michael William Kahelin		
Docket No.:	1023-203US01		
Title:	DELIVERING GENETIC MATERIAL TO A STIMULATION SITE		

CERTIFICATE UNDER 37 CFR 1.8 I hereby certify that this correspondence is being transmitted via the United States Patent and Trademark Office electronic filing system on June 18, 2010.

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APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450,
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Sir:

This is an Appeal Brief in support of an appeal from the nonfinal Office Action dated February 19, 2010, which rejected claims 21–24, 26, 29–33, 35–42, and 46-54. Claims 21–24, 26, 29–33, 35–42, and 46 were rejected for at least the second time in the nonfinal Office Action dated February 19, 2010. The Notice of Appeal was filed on April 21, 2010. The period for filing this Brief runs through June 21, 2010.

No fee is believed at this time. A first Notice of Appeal was filed on March 23, 2009, and on May 8, 2009, Appellant filed an Appeal Brief in support of the appeal. Prosecution was reopened following the filing of the Appeal Brief. Thereafter, on April 21, 2010, Appellant filed a second Notice of Appeal. Accordingly, the previously paid fee for submitting an Appeal Brief

may be applied to the present Appeal Brief. Please charge any additional fees that may be required or credit any overpayment to Deposit Account No. 50-1778.

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REAL PARTY OF INTEREST

The Real Party of Interest is Medtronic, Inc. of Minneapolis, Minnesota.

RELATED APPEALS AND INTERFERENCES

A first Notice of Appeal was filed on March 23, 2009 for the above-referenced patent application (U.S. Patent Application Serial No. 10/663,570), which is the subject of the present appeal. Prosecution was reopened following the filing of the first Notice of Appeal. The previously initiated appeal for U.S. Patent Application Serial No. 10/663,570 was withdrawn at the time prosecution was reopened, and, therefore, there are no related appeals pending. In addition, there are no related interferences for U.S. Patent Application Serial No. 10/663,570.

STATUS OF CLAIMS

Claims 21–24, 26, 29–33, 35–42, and 46–54 are pending and are the subject of this appeal. Claims 21–24, 26, 29–33, 35–42, and 46–54 are set forth in Appendix A. Originally filed claims 5–8 were canceled in an Amendment filed on August 4, 2006. In addition, originally filed claims 11 and 27 were canceled in an Amendment filed on June 28, 2007, and originally filed claims 20, 25, 28, and 34 were canceled in an Amendment filed on October 29, 2007. Claims 40–45 were added by way of an Amendment filed on August 4, 2006. Claim 46 was added by way of an Amendment filed on November 7, 2008. Claims 1–4, 9, 10, 12–19, and 43–45 were canceled in an Amendment filed on November 7, 2008 as being drawn to a nonelected invention. Claims 47–54 were added by way of an Amendment filed on October 20, 2009

Claims 21–24, 26, 29–33, 35–42, and 46–54 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Soykan et al. (U.S. Patent No. 6,151,525, hereinafter "Soykan") in view of Heil, Jr. et al. (U.S. Patent No. 4,819,662, hereinafter "Heil") and Girouard et al. (U.S. Patent Application Publication No. 2004/0158289, hereinafter "Girouard").

STATUS OF AMENDMENTS

The claims on appeal are those submitted in the Amendment filed on October 20, 2009. The Office Action dated February 19, 2010 indicates that the Examiner entered the Amendment filed on October 20, 2009. No amendments were submitted after the Office Action dated February 19, 2010.

SUMMARY OF CLAIMED SUBJECT MATTER

In general, Appellant's disclosure relates to delivering genetic material to tissue at a stimulation site to increase conductivity of the tissue.[1]

Independent claim 1 is directed to a medical lead[2] including a lead body,[3] a porous electrode[4] mounted on the lead body to deliver electrical stimulation[5] to a stimulation site[6] within a patient, a genetic material[7] that causes expression of at least one of a connexin or a gap-junction by tissue[8] at the stimulation site,[9] wherein the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue,[10] and a chamber body[11] that defines a chamber. The chamber contains a polymeric matrix[12] that absorbs[13] the genetic material[14] and degrades to elute[15] the genetic material to tissue at the stimulation site via the porous electrode.[16]

Independent claim 35 is direct to a method comprising introducing genetic material to a polymeric matrix,[17] and placing the matrix into a chamber formed by a chamber body[18] of a medical lead[19] for elution of the genetic material to tissue of a patient at a stimulation site.[20] The

[1] Appellant's disclosure at p. 2, ll. 6–11.
[2] *Id.* at p. 4, ll. 15 and 16, and lead 18 shown in FIG. 1 and lead 50 shown in FIGS. 3A and 3B.
[3] *Id.* at p. 5, ll. 18–20, and lead body 36 shown in FIG. 2 and lead body 52 shown in FIGS. 3A and 3B.
[4] *Id.* at p. 7, ll. 1–5, and electrode 54 shown in FIGS. 3A and 3B.
[5] *Id.* at p. 8, ll. 23–25.
[6] *Id.* at p. 8, ll. 23–25, and stimulation site 12 shown in FIGS. 1 and 2.
[7] *Id.* at p. 4, ll. 15–19.
[8] *Id.* at p. 6, ll. 6–9.
[9] *Id.* at p. 4, ll. 20–31.
[10] *Id.* at p. 4, ll. 23–26 and p. 6, ll. 7–9.
[11] *Id.* at p. 6, ll. 1 and 2, and chamber body 56 shown in FIGS. 3A and 3B.
[12] *Id.* at p. 7, ll. 12–16, and matrix 58 shown in FIG. 3A.
[13] *Id.* at p. 7, ll. 13 and 14.
[14] *Id.* at p. 7, ll. 12 and 13.
[15] *Id.* at p. 7, ll. 14 and 15.
[16] *Id.* at p. 7, ll. 14–16.
[17] *Id.* at p. 7, ll. 6–11, and block 70 shown in FIG. 4.
[18] *Id.* at p. 7, ll. 12–14.
[19] *Id.* at p. 4, ll. 15 and 16, and lead 18 shown in FIG. 1 and lead 50 shown in FIGS. 3A and 3B.

genetic material is adapted to cause expression of at least one of a connexin[21] or a gap-junction[22] by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site.[23] According to claim 35, the medical lead includes a porous electrode,[24] and the matrix elutes the genetic material to the stimulation site via the porous electrode.[25]

Independent claim 47 is directed to a medical lead[26] comprising a lead body, [27] a porous electrode[28] mounted on the lead body, where the porous electrode delivers electrical stimulation[29] to a stimulation site[30] within a patient, a genetic material, [31] and a chamber body[32] that defines a chamber. The genetic material causes expression of at least one of a connexin or a gap-junction[33] by the tissue at the stimulation site,[34] and the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue. [35] The chamber contains a polymeric matrix[36] that absorbs[37] the genetic material[38] and elutes[39] the genetic material to tissue at the stimulation site via the porous electrode.[40] Claim 47 specifies that the polymeric matrix comprises extracellular collagen.[41]

GROUND OF REJECTION TO BE REVIEWED ON APPEAL

Appellant submits the following ground of rejection to be reviewed on appeal: the rejection of claims 21–24, 26, 29–33, 35–42, and 46–57 under 35 U.S.C. § 103(a) as allegedly being obvious over Soykan in view of Heil and Girouard.

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[20] *Id.* at p. 7, ll. 13–15.
[21] *Id.* at p. 4, ll. 23–26.
[22] *Id.*
[23] *Id.*
[24] *Id.* at p. 7, ll. 1–5, and electrode 54 shown in FIGS. 3A and 3B.
[25] *Id.* at p. 7, ll. 13–15.
[26] *Id.* at p. 4, ll. 15 and 16, and lead 18 shown in FIG. 1 and lead 50 shown in FIGS. 3A and 3B.
[27] *Id.* at p. 5, ll. 18–20, and lead body 36 shown in FIG. 2 and lead body 52 shown in FIGS. 3A and 3B.
[28] *Id.* at p. 7, ll. 1–5, and electrode 54 shown in FIGS. 3A and 3B.
[29] *Id.* at p. 8, ll. 23–25.
[30] *Id.* at p. 8, ll. 23–25, and stimulation site 12 shown in FIGS. 1 and 2.
[31] *Id.* at p. 4, ll. 15–19.
[32] *Id.* at p. 6, ll. 1 and 2, and chamber body 56 shown in FIGS. 3A and 3B.
[33] *Id.* at p. 6, ll. 6–9.
[34] *Id.* at p. 4, ll. 20–31.
[35] *Id.* at p. 4, ll. 23–26 and p. 6, ll. 7–9.
[36] *Id.* at p. 7, ll. 12–16, and matrix 58 shown in FIG. 3A.
[37] *Id.* at p. 7, ll. 13 and 14.
[38] *Id.* at p. 7, ll. 12 and 13.
[39] *Id.* at p. 7, ll. 14 and 15.
[40] *Id.* at p. 7, ll. 14–16.
[41] *Id.* at p. 7, ll. 15 and 16.

ARGUMENT

Appellant respectfully requests reversal of the rejection of claims 21–24, 26, 29–33, 35–42, and 46–57 by the Board of Patent Appeals based on the arguments below. For the ground of rejection to be reviewed on appeal, Appellant respectfully requests separate review of each set of claims argued under separate headings. For at least the reasons presented below, the Examiner has failed to establish a *prima facie* case of obviousness with respect to Appellant's claims 21–24, 26, 29–33, 35–42, and 46–57.

GROUND OF REJECTION TO BE REVIEWED ON APPEAL - THE REJECTION OF CLAIMS 21–24, 26, 29–33, 35–42, and 46–57 UNDER 35 U.S.C. § 103(a)

Claims 21–24, 26, 29–33, 35–42, and 46–57 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Soykan in view of Heil and Girouard. For at least the reasons discussed below, the rejection of claims 21–24, 26, 29–33, 35–42, and 46–57 as being obvious over Soykan in view of Heil and Girouard should be reversed.

CLAIMS 21–24, 26, AND 29–33

Soykan in view of Heil and Girouard lacks any teaching that would have suggested a medical lead that includes a porous electrode, a genetic material that causes expression of at least one of a connexin or a gap-junction by tissue at the stimulation site, where the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue, and a chamber body that defines a chamber containing a polymeric matrix that absorbs the genetic material and degrades to elute the genetic material to tissue at the stimulation site via the porous electrode, as recited by independent claim 21.

In support of the rejection of independent claim 21 as being obvious over Soykan in view of Heil and Girouard, the Examiner stated that Soykan discloses a lead that delivers electrical stimulation to a tissue site and elutes genetic material from a polymeric matrix.[42] The Examiner acknowledged that Soykan does not disclose or suggest required elements of Appellant's claimed lead, such as a chamber that elutes material from a porous electrode or a genetic material that is adapted to cause expression of at least one of connexin or a gap junction.[43] The Examiner looked to both Heil and Girouard in an attempt to cure the identified deficiencies in the Soykan

[42] Office Action dated February 19, 2010 at p. 2, item 4.
[43] *Id.* at p. 3, item 4.

reference. In particular, the Examiner asserted that Heil discloses "a lead with a removable chamber that elutes substances through a porous electrode" and Girouard discloses "providing a cardiac therapy comprising delivering connexin."[44]

The Examiner reasoned that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Soykan in view of Heil and Girouard "for the purpose of providing controlled release of pharmacological agents at the site of electrical therapy and providing a cardiac therapy comprising delivering connexin for the purpose of repairing damaged heart tissue."[45] The Examiner's conclusion of obviousness is erroneous. The medical lead of independent claim 21 is not obvious over Soykan in view of Heil and Girouard.

In order to support a rejection under 35 U.S.C. § 103(a), the Examiner must clearly articulate the reasons why the claimed invention would have been obvious.[46] In the present rejection of independent claim 21, the Examiner has failed to establish an apparent reason with a rational underpinning for modifying Soykan in view of Heil and Girouard, and, thus, failed to establish a *prima facie* case of obviousness of claim 21. While the Examiner stated that one having ordinary skill in the art would have looked to Heil to modify Soykan in order to provide "controlled release of pharmacological agents at the site of electrical therapy,"[47] this purported reason lacks a rational underpinning.[48] This statement appears to overlook the fact that the system disclosed by Soykan already provides controlled release of a genetic material at the site of electrical therapy. For example, Soykan discloses coating or otherwise incorporating a genetic material into a carrier, which may be an electrical stimulation device.[49] Soykan discloses that the genetic material may be delivered in a polymeric matrix.[50] According to the Examiner, "[t]he level of cross-linking [of a matrix] is inherently proportional to the release rate."[51]

The Examiner asserted that Soykan "is silent as to precisely where on or in the electrical stimulation device the carrier resides," and, therefore, one having ordinary skill in the art would have looked to Heil for a carrier configuration.[52] Contrary to these assertions, Soykan discloses

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[44] *Id.*
[45] *Id.* at pp. 3 and 4, item 4.
[46] *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) and MPEP 2141(III).
[47] Final Office Action dated January 23, 2009 at pp. 3 and 4, item 4.
[48] *See* MPEP 2142, *citing In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) ("[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.")
[49] Soykan at col. 11, ll. 5–7.
[50] *Id.* at col. 11, ll. 15–16.
[51] Final Office Action dated January 23, 2009 at p. 4, item 6.
[52] Examiner's Answer dated August 20, 2009, page 10, item 10 ("Response to Arguments").

that genetic material may be coated on or otherwise incorporated into a carrier, such as an electrical stimulator capsule or a catheter,[53] and, therefore, Soykan discloses a carrier configuration. Soykan also discloses injection of the genetic material into a patient separately from an electrical stimulation device, e.g., via a catheter.[54] Absent access to Appellant's disclosure, one having ordinary skill in the art would not have had any apparent reason to incorporate the electrical stimulator coating disclosed by Soykan into a chamber of the lead disclosed by Heil. A coating disclosed by Soykan differs in operation from the chamber delivery system disclosed by Heil. Thus, the modification to Soykan in view of Heil proposed by the Examiner would change the principle of operation of the coating disclosed by Soykan, and, therefore, would not have been obvious to one having ordinary skill in the art at the time of Appellant's invention.[55]

Heil does not provide any indication that the porous electrode is advantageous over the coating disclosed by Soykan for releasing a genetic material, or provides some expected beneficial result over the coating disclosed by Soykan. Accordingly, the cited art does not support the Examiner's proposed reason that one having ordinary skill in the art would have had modified Soykan in view of Heil. Indeed, absent access to Appellant's disclosure, there is no apparent reason why one having ordinary skill in the art would have looked to Heil, which relates to a drug eluting lead, to modify Soykan, which relates to a device that releases a genetic material, in the manner suggested by the Examiner.

The Examiner asserted that the one having ordinary skill in the art would have been motivated to modify the system disclosed by Soykan by providing the agent at the site of electrical stimulation, as asserted to be disclosed by Heil, "because the cells that are the target of the therapeutic agent are the same cells that are the target of the electrical therapy."[56] This assertion by the Examiner is an improper basis for the obviousness rejection because it mischaracterizes the Soykan disclosure. For example, the Examiner's proposed reason for modifying Soykan in view of Heil overlooks the fact that Soykan already discloses an electrical stimulation device that carries genetic material, e.g., as a coating.[57] Thus, Soykan appears to disclose a system for providing a genetic material at the site of electrical stimulation.

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[53] Soykan at col. 11, ll. 5–7 and col. 12, ll. 33–40.
[54] *Id.* at col. 12, ll. 60–65.
[55] *See* MPEP 2143.01(VI), *citing In re Ratti*, 270 F.2d 810 (CCPA 349).
[56] Examiner's Answer dated August 20, 2009 at p. 11.
[57] Soykan at col. 11, ll. 5–7.

According to the Examiner, a rational reason need not be shown for modifying Soykan with Heil because "modifying Soykan's genetic material-eluting cardiac device with Heil's known prior art drug-eluting cardiac device is a simple substitution of one known element for another to obtain the predictable results of controlled release of a therapeutic agent."[58] However, even in the case of a claim rejection based on the "predictable results" rationale, identification of a reason why a person of ordinary skill would have combined the elements in the manner proposed by the Examiner is important.[59] The Examiner has failed to identify a rational reason why a person of ordinary skill would have combined the Soykan system and the Heil electrode. Therefore, the Examiner failed to establish a *prima facie* case of obviousness with respect to independent claim 21.

The modification of the Soykan system to include the porous electrode and recess (for retaining a matrix including a therapeutic drug) disclosed by Heil is not merely a simple substitution of one known element for another, nor does the modification proposed by the Examiner necessarily provide a "predictable result" of "controlled release of a therapeutic agent," as asserted by the Examiner.[60] A drug, as disclosed by Heil, and a genetic material, as disclosed by Soykan, may have different purposes and different properties. As a result, there may be different considerations and objectives for elution of a drug versus elution of a genetic material. As an example of the differences between a drug and a genetic material, Appellant has recognized that expression of at least one of connexin or a gap-junction may provide advantages over elution of a drug, such as a desired effect that lasts longer and is more localized than that of drug.[61]

In the final Office Action, the Examiner agreed that drugs and genetic materials are different, but asserted that the differences relate to different therapeutic effect and "do not pertain to the mechanical diffusion of these substances from a porous electrode."[62] The Examiner asserted that because the electrode disclosed by Heil "is porous enough to allow for 'free fluid flow,'" the electrode "is capable of eluting both drugs and genetic material."[63] Appellant disagrees that different therapeutic effects of drugs and genetic materials are irrelevant to the diffusion of the materials from a porous electrode. The different therapeutic effects are

[58] Final Office Action dated January 23, 2009 at p. 6, item 12 (Response to Arguments section).
[59] MPEP 2143, *citing KSR Int'l Co.*, 550 U.S. at 418.
[60] Final Office Action dated January 23, 2009 at p. 6, item 12 (Response to Arguments section).
[61] Appellant's originally-filed disclosure at p. 2, ll. 6–13.
[62] Final Office Action dated January 23, 2009 at p. 5, item 11 (Response to Arguments section).
[63] *Id.*

necessarily considered when determining how the drug or genetic material should be eluted. As indicated above, Appellant has recognized that expression of at least one of connexin or a gap-junction may have a desired effect that lasts longer and is more localized than that of drug.[64] Thus, the desirable diffusion rates for providing the desired effect may differ between a drug and a genetic material. The references relied on by the Examiner fail to provide any indication that the "free fluid flow"[65] provided by the Heil porous electrode is sufficient or even useful for the elution of a genetic material at a desirable rate for the particular application disclosed by Soykan.

References may only be modified to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success.[66] Neither the Heil nor Soykan disclosures provide reasonable support for asserting that modifying Soykan in view of Heil to include a matrix that elutes a genetic material to tissue at a stimulation site via a porous electrode would reasonably be expected to be successful. For example, the cited art fails to provide a reasonable basis for concluding that that elution of a genetic material via a porous electrode that also delivers electrical stimulation to tissue would be successful in causing expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site. Heil only discusses a matrix that elutes a drug, and does not contemplate elution of a genetic material, much less elution of a genetic material that increases the conductivity of tissue at the stimulation site. Thus, there is no basis for asserting that it would have been obvious to one having ordinary skill in the art to modify the Soykan system to elute a genetic material via the porous electrode disclosed by Heil.

The Examiner also failed to provide any articulated reasoning for why one having ordinary skill in the art would have looked to Girouard to modify Soykan. The Examiner stated that one having ordinary skill in the art would have looked to Girouard to modify Soykan in order to provide "a cardiac therapy comprising delivering connexin for the purpose of repairing damaged heart tissue."[67] This rationale, however, is circular and lacks a rational underpinning. The rationale provided by the Examiner fails to identify a reason that would have even prompted a person having ordinary skill in the art to even modify the type of genetic material disclosed by Soykan. Girouard does not provide any indication that connexin is advantageous over the genetic material disclosed by Soykan, or provides some expected beneficial result over the coating disclosed by Soykan.

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[64] Appellant's originally-filed disclosure at p. 2, ll. 6–13.
[65] Heil at col. 2, ll. 38–41.
[66] MPEP 2143.02 (I).
[67] Final Office Action dated January 23, 2009 at p. 3, item 4.

According to the Examiner, "modifying Soykan's cardiac-repairing genetic material with Girouard's known prior art cardiac-repairing genetic material is a simple substitution of one known element for another to obtain the predictable results of repairing damaged heart tissue."[68] This assertion is erroneous. As described in further detail below, Girouard proposes the use of a genetic material for a different purpose than Soykan. Thus, modifying the Soykan system to clute a genetic material that causes expression of connexin by tissue would have required more than a simple substitution of one known element for another.

The Examiner asserted that modifying Soykan in view of a genetic material disclosed by Girouard involves a simple substitution because both Soykan and Girouard disclose the use of a "cardiac-repairing genetic material." However, Soykan is not merely directed at repairing damaged heart tissue. Instead, Soykan discloses the use of genetic material to convert noncontracting cells to contracting cells in an infarct zone of a patient's myocardium, i.e., *in vivo*.[69] On the other hand, Girouard discloses a transgene that encodes, e.g., connexin-40, connexin-42, and connexin-43, to condition donor cells *in vitro*, prior to administration of the donor cells into a region of injured tissue of the patient.[70] In particular, Girouard uses the genetic material to subject donor cells to exogenous agents, such as differentiation factors, growth factors, and the like.[71] The donor cells are conditioned outside of the patient, and then subsequently introduced into the tissue region to be treated. Thus, while Girouard discloses providing cell therapy of living tissue, Girouard is only directed to the use of exogenous cells,[72] which may be conditioned using genetic material. The use of genetic material to condition exogenous cells by Girouard is contrary to Soykan, which discloses the conversion of cells in an infarct zone within the patient using genetic material.

In response to Appellant's remarks presented in the first Appeal Brief filed on May 8, 2009, the Examiner asserted that "Girouard recognizes that the vectors may be applied *in vitro* or *in vivo*," and, therefore, an artisan of ordinary skill "could have predictably applied Girouard's teaching of providing genetic material that causes the expression of connexin to Soykan's' system."[73] This statement is a misrepresentation of the Girouard disclosure. In a definition section provided by Girouard, Girouard generally defines a "vector" or "construct" as referring

[68] *Id.* at p. 6, item 13 (Response to Arguments section).
[69] Soykan at col. 7, ll. 54–60.
[70] Girouard at ¶¶ [0076], [0129], and [0146].
[71] *Id.* at ¶ [0146].
[72] *Id.* at Abstract.
[73] Examiner's Answer dated August 20, 2009 at p. 12.

to a macromolecule or a complex of molecules comprising a polynucleotide to be delivered to a host cell either *in vitro* or *in vivo*.[74] It is improper for the Examiner to rely on this definition to assert that all genetic material disclosed by Girouard is configured to be applied *in vitro* and *in vivo*.

Appellant's independent claim 21 recites a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site. With respect to the transgene that encodes connexin-42 or connexin-43, Girouard discloses that the transgene is used to biologically condition donor cells by subjecting the donor cells to exogenous agents, such as transgenes.[75] As discussed above, Girouard only discloses subjecting donor cells to exogenous agents, such as transgenes, *in vitro*.[76] For example, Girouard explicitly states that "donor cells are condition in vitro to introduce one or more desirable gene products (transgenes) to the cells."[77] At no time does Girouard disclose or suggest that donor cells may be subjected to transgenes that encodes connexin-42 or connexin-43 *in vivo*, as the Examiner asserts. With respect to the *in vivo* cell therapy techniques, Girouard merely states that donor cells can be delivered to a region of tissue to be treated. Girouard further discloses that in a different embodiment, there may be an additional step of preparing the donor cells before administering the cell therapy, such as by conditioning the donor cells *in vitro* to introduce one or more desirable gene products to the cells.[78] This clearly indicates that Girouard does not contemplate the delivery of a genetic material to a tissue site.

For at least these reasons, Girouard does not support the Examiner's assertion that all genetic material disclosed by Girouard is configured to be applied *in vitro* and *in vivo*. The rejection of independent claim 21 should be reversed on the at least the ground that the Examiner has mischaracterized the Girouard disclosure to support the rejection of independent claim 21.

Neither Soykan nor Girouard provides any indication that expression of connexin, which takes place *ex vivo* in the Girouard reference, may be simply substituted in the *in vivo* technique disclosed by Soykan, as asserted by the Examiner.[79] Moreover, Girouard does not even contemplate delivering a genetic material that causes expression of connexin to an infarct zone of a heart of a patient to convert noncontracting cells (e.g., fibroblasts) to contracting cells (e.g.,

[74] Girouard at ¶ [0044].
[75] *Id.* at ¶ [0144].
[76] *Id.* at ¶ [0129].
[77] *Id.* at ¶ [0076].
[78] *Id.*
[79] Final Office Action dated January 23, 2009 at p. 6, item 13 (Response to Arguments section).

myoblasts) *in vivo* to reverse damage to necrotic heart muscle,[80] as required by Soykan. Instead, Girouard merely contemplates the use of connexin to condition exogenous cells *in vitro*. According to Girouard, exogenous cells are subsequently introduced into other cells.[81] Therefore, exogenous cells are different than the noncontractile cells in an infarct zone, as disclosed by Soykan. For at least these reasons, the Examiner's assertion that the modification of Soykan in view of Girouard is obvious on the basis that it involves a simple substitution of one known element for another is erroneous.

Even if Soykan was modified to include the genetic material disclosed by Girouard, the resulting system would not include each and every element of claim 21, such as a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site and a chamber body that contains a polymeric matrix that absorbs the genetic material and degrades to elute the genetic material to tissue at the stimulation site via the porous electrode. None of the cited references disclose or suggest the delivery of such a genetic material to a tissue at a stimulation site. Thus, even if the Examiner is relying on Soykan rather than Girouard as disclosing providing genetic material directly to cells within the heart,[82] one having ordinary skill in the art at the time of Appellant's invention would not have had any apparent reason, absent access to Appellant's disclosure, to substitute a genetic material disclosed by Soykan with the genetic material disclosed by Girouard, which is disclosed to be delivered to cells *ex vivo*.

It would not have been obvious to one having ordinary skill in the art at the time the invention was made to modify Soykan in view of either Heil or Girouard to arrive at the lead of Appellant's independent claim 21. According to the MPEP, a "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."[83] Thus, in order to rely on the "predictable result" rationale to support the rejection of Appellant's independent claim 21, the proposed combination must combine the "elements" of the cited art according to known methods. Moreover, according to MPEP 2141, when considering obviousness of a combination of elements of cited references, the operative question

[80] Soykan at col. 4, ll. 33–35 and ll. 49–56.
[81] Girouard at ¶ [0056].
[82] Examiner's Answer at p. 12.
[83] MPEP 2141, *citing KSR Int'l Co.*, 550 U.S. at 416.

is "whether the improvement is more than the predictable use of prior art elements according to their established functions."[84]

As established above, the combination of Soykan, Heil, and Girouard proposed by the Examiner changes the established functions of the cited references. Accordingly, Appellant's claim 21 is not obvious in view of the cited references. Soykan discloses an implantable system that converts fibroblasts to myoblasts *in vivo* by delivering specific genetic materials, which Soykan fails to disclose or suggest cause expression of at least one of a connexin or a gap-junction, as required by claim 21.[85] The Examiner asserted that it would have been obvious to substitute a genetic material (causing expression of connexin) disclosed by Girouard in the Soykan system. However, Girouard does not use the genetic material *in vivo* for the same function as the Soykan genetic material. Instead, Girouard uses the genetic material that causes expression of connexin to condition exogenous cells *in vitro*, prior to introduction in the patient. Thus, the Examiner's proposed use of connexin changes the function of connexin established by Girouard.

The asserted combination of elements of the references cited by the Examiner in support of the rejection of independent claim 21 is more than a mere predictable use of the elements according to the established functions. Indeed, modifying the Soykan system in view of Girouard to include a genetic material that causes expression of a connexin requires a change to the Girouard system, thereby rendering the combination nonobvious. The cited art fails to provide any indication that a genetic material that causes expression of a connexin (as disclosed by Girouard) is suitable for use *in vivo* to convert noncontractile cells to contractile cells, as required by Soykan. The *in vitro* use of the genetic material that causes expression of a connexin disclosed by Girouard differs from the *in vivo* technique disclosed by Soykan. For at least these reasons, even if Soykan, Heil, and Girouard disclose each and every element of the lead of Appellant's claim 21, an assertion with which Appellant does not agree, Appellant's claimed lead is more than just the predictable use of the elements of the cited references.

Appellant has recognized that delivering a genetic material that causes expression of a connexin or a gap-junction by tissue at a stimulation site increases the conductivity of the tissue at the stimulation site, thereby forming a virtual biological electrode.[86] By delivering the genetic

[84] MPEP 2141, *citing KSR Int'l Co.*, 550 U.S. at 417.
[85] Soykan at col. 7, ll. 53–60 and col. 8, ll. 1–5.
[86] Appellant's disclosure at p. 4, ll. 20–29.

material via a porous electrode of a lead, the virtual biological electrode is in contact with the electrode of the lead. The delivery of pacing pulses by the electrode of the lead is facilitated by the virtual biological electrode at the stimulation site, which may, e.g., result in the capture of a heart of the patient at lower pacing pulse amplitudes.[87] In general, Appellant has recognized that the expression of connexin or a gap-junction by tissue at a stimulation site improves the characteristics of the electrode-tissue interface, which may help reduce the intensity of stimulation signals that are necessary to achieve a desired effect.[88] Reduction of the stimulation intensity is useful for prolonging the life of the battery of a medical device that delivers the stimulation therapy. The lead of claim 21 facilitates the delivery of the genetic material to achieve such benefits. The cited references fail to disclose or suggest the lead of claim 21.

Based on the lack of disclosure within Soykan, Heil, and Girouard regarding the possibility of eluting a genetic material that causes expression of a connexin or a gap-junction via a porous electrode, Soykan in view of Heil and Girouard fails to render Appellant's independent claim 21 obvious. In the present application, the gap between the cited art and the lead of Appellant's claim 21 is so great as to render independent claim 21 nonobvious to one having ordinary skill in the art.[89]

For at least these reasons, the Examiner has failed to establish a *prima facie* case for non-patentability of Appellant's independent claim 21 under 35 U.S.C. § 103(a). Claims 22–24, 26, and 29–33 depend from claim 21 and are patentable over Soykan in view of Heil and Girouard for at least the reasons discussed above with respect to independent claims 21.

[87] *Id.* at p. 4, ll. 27–31.
[88] Appellant's disclosure at p. 2, ll. 6–10.
[89] *See* MPEP 2141, *citing Dann v. Johnston*, 425 U.S. 219, 230 (1976).

CLAIM 46

Claim 46 specifies that the lead of independent claim 21 includes a chamber body defining a chamber that contains a polymeric matrix that absorbs a genetic material and elutes the genetic material to tissue at a stimulation site within a patient via a porous electrode, where the genetic material is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site and create a preferential conduction pathway between the stimulation site and at least one of a bundle of His or a Purkinje fiber of a heart of the patient. The cited art fails to disclose or suggest the lead of claim 46.

In support of the rejection of claim 46, the Examiner stated that claim 46 is directed to an inherent feature of Soykan and reasoned that "[b]ecause Soykan is in effect creating new contractile tissue around the stimulation device, this inherently creates a new arbitrary 'preferred conduction pathway.'"[90] The Examiner is relying on an improper finding of an inherent disclosure in Soykan to support the rejection of claim 46. The creation of "new contractile tissue" around a stimulation device does not in any way suggest that the "new contractile tissue" defines a pathway that is more conductive than another.

The fact that a certain characteristic may be present in the prior art is not sufficient to establish the inherency of that result or characteristic.[91] The Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.[92] No reasonable support has been provided for the determination that the conversion of noncontractile tissue to contractile tissue in an infarct zone, as disclosed by Soykan, necessarily creates a preferential conduction pathway between the stimulation site and at least one of a bundle of His or a Purkinje fiber of a heart of the patient. Rather, the formation of a conduction pathway that is the same as or less preferred to another pathway between a stimulation site and at least one of a bundle of His or a Purkinje fiber of the heart are just as likely in view of the lack of description provided by the Soykan reference. Accordingly, Appellant submits that the allegedly inherent characteristic does not necessarily flow from the teachings of Soykan, and that the Examiner has relied on an improper finding of inherent disclosure in Soykan to reject independent claim 46.

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[90] Final Office Action dated January 23, 2009 at p. 7, item 15 (Response to Arguments section).
[91] *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993); MPEP § 2112.
[92] *Ex parte Levy*, 17 USPQ.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original); MPEP 2112.

While Soykan discloses converting noncontractile cells to contractile cells with nucleic acid,[93] Soykan does disclose or even suggest that such conversion to contractile cells necessarily results in the creation of a preferential conduction pathway between at least one of a bundle of His or a Purkinje fiber of a heart of the patient. A preferential conduction pathway clearly requires a pathway that is more preferred over another pathway. The conversion of noncontractile cells to contractile cells may improve the conduction pathway compared to the pathway that existed prior to the conversion of the cells to contractile cells. However, this improvement in the conduction pathway does not necessarily result in a pathway that is more preferred over other pathways between the stimulation site and the bundle of His or a Purkinje fiber of a heart of the patient.

The Examiner asserted that because the current or action potential "necessarily follows a new path because of the new contractile tissue, this path is 'preferred' by the current or action potential to the previous path."[94] The Examiner's interpretation of the phrase "preferential conduction pathway" is unreasonable when Appellant's specification is properly considered. As stated by the Federal Circuit in *Phillips v. AWH Corp.*, "[t]he Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction 'in light of the specification as it would be interpreted by one of ordinary skill in the art.'"[95] Thus, "[d]uring patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification."[96] The Examiner's interpretation of "preferential conduction pathway" to include a pathway that is preferred relative to the same pathway at some previous point in time is unreasonable and inconsistent with Appellant's specification. In view of Appellant's specification, it is clear that a preferential conduction pathway is a pathway that is preferred relative to other existing and available pathways for electrical conduction.

Appellant's claim 46 recognizes that delivering a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site can form a preferential conduction pathway to the bundle of His or a Purkinje fiber by increasing the conductivity of the tissue relative to other

[93] Soykan at col. 7, ll. 53–60.
[94] Examiner's Answer dated August 20, 2009 at p. 13.
[95] 415 F.3d 1303, 1316 (Fed. Cir. 2005), *citing In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364, 70 USPQ2d 1827 (Fed. Cir. 2004).
[96] *See* MPEP § 2111.

(e.g., adjacent) tissue through which the stimulation may also traverse.[97] Soykan does not inherently disclose that the conversion of noncontractile cells to contractile cells necessarily results in the creation of such a preferential conduction pathway.

For at least these reasons, the Examiner has failed to establish a *prima facie* case for non-patentability of Appellant's claim 46 under 35 U.S.C. § 103(a), and the rejection of claim 46 should be reversed.

CLAIMS 35–42

Independent claim 35 is directed to a method that comprises introducing genetic material to a polymeric matrix and placing the matrix into a chamber formed by a chamber body of a medical lead for elution of genetic material to tissue of a patient at a stimulation site, where the genetic material is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site, and where the matrix elutes the genetic material to the stimulation site via a porous electrode of the medical lead. Claim 35 was rejected under 35 U.S.C. § 103(a) as being obvious over Soykan in view of Heil and Girouard.

As discussed above with respect to independent claim 21, Soykan in view of Heil and Girouard fails to disclose or suggest a medical lead that includes a matrix with a genetic material that is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site, whereby the matrix elutes the genetic material to the stimulation site via a porous electrode of the lead. Thus, for similar reasons, the cited references fail to disclose or suggest the method of claim 35, which requires introducing a genetic material to a polymeric matrix and placing the matrix into a chamber formed by a chamber body of a medical lead.

For at least these reasons, the Examiner has failed to establish a *prima facie* case for non-patentability of Appellant's independent claim 35 under 35 U.S.C. § 103(a). Claims 36–42 depend from claim 35 and are patentable over Soykan in view of Heil and Girouard for at least the reasons discussed above with respect to independent claim 35

[97] *See* Appellant's disclosure at p. 6, ll. 8–12.

CLAIMS 47–54

Independent claim 47 is directed to a lead that comprises a lead body, a porous electrode mounted on the lead body, wherein the porous electrode delivers electrical stimulation to a stimulation site within a patient, a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site, wherein the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue, and a chamber body that defines a chamber containing a polymeric matrix that absorbs the genetic material and elutes the genetic material to tissue at the stimulation site via the porous electrode, wherein the polymeric matrix comprises extracellular collagen.

As discussed above with respect to independent claim 21, Soykan in view of Heil and Girouard fails to disclose or suggest a medical lead that includes a matrix with a genetic material that is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site, whereby the matrix elutes the genetic material to the stimulation site via a porous electrode of the lead. Thus, for similar reasons, the cited references fail to disclose or suggest the lead of claim 47.

Claims 48–53 depend from independent claim 47 and are patentable over the cited references for at least the reasons discussed with respect to claim 47.

CLAIM 54

Claim 54 depends from independent claim 47 and specifies that the genetic material is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site and create a preferential conduction pathway between the stimulation site and at least one of a bundle of His or a Purkinje fiber of a heart of the patient. Soykan in view of Heil and Girouard fails to disclose the lead of claim 54.

For at least the reasons discussed with respect to claim 46, the Examiner relied on an improper assertion that Soykan inherently discloses that the conversion of noncontractile cells to contractile cells necessarily results in the creation of the preferential conduction pathway recited in Appellant's claim 54. Furthermore, the Examiner's interpretation of claim 54 is unreasonable and inconsistent with Appellant's disclosure. For at least these reasons, the rejection of claim 54 based on Soykan in view of Heil and Girouard should be reversed.

For the foregoing reasons, reversal of the rejection of claims 21–24, 26, 29–33, 35–42, and 46–54 under 35 U.S.C. § 103(a) as being unpatentable over Soykan in view of Heil and Girouard is respectfully requested.

CONCLUSION

The Examiner has failed to meet the burden of establishing a *prima facie* case of nonpatentability with respect to Appellant's claims 21–24, 26, 29–33, 35–42, and 46–54. Appellant respectfully requests review of the rejections addressed above, and reversal of all pending rejections. In addition, Appellant respectfully requests separate review by the Board for each set of claims argued under separate headings for the ground of rejection addressed above.

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APPENDIX A

THE CLAIMS ON APPEAL

Claim 21: A medical lead comprising:

a lead body;

a porous electrode mounted on the lead body to deliver electrical stimulation to a stimulation site within a patient;

a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site, wherein the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue; and

a chamber body that defines a chamber, the chamber containing a polymeric matrix that absorbs the genetic material and degrades to elute the genetic material to tissue at the stimulation site via the porous electrode.

Claim 22: The medical lead of claim 21, wherein the matrix comprises extracellular collagen.

Claim 23: The medical lead of claim 21, wherein the matrix is cross-linked, and degrades to elute the absorbed genetic material at a degradation rate that is a function of the cross-linking.

Claim 24: The medical lead of claim 21, wherein the chamber body is separable from the lead for loading with the matrix and the genetic material.

Claim 26: The medical lead of claim 21, wherein the genetic material comprises at least one of a viral vector, a liposomal vector or plasmid deoxyribonucleic acid (DNA).

Claim 29: The medical lead of claim 21, wherein the genetic material is adapted to cause expression of connexin-43 by the tissue at the stimulation site.

Claim 30: The medical lead of claim 21, wherein the genetic material is adapted to cause expression of at least one of a metalloproteinase, an anti-inflammatory agent or an immunosuppressant agent.

Claim 31: The medical lead of claim 30, wherein the genetic material is adapted to cause expression of IκB.

Claim 32: The medical lead of claim 21, wherein the electrode is implantable within the patient.

Claim 33: The medical lead of claim 32, wherein the tissue at the stimulation site comprises cardiac tissue.

Claim 35: A method comprising:

introducing genetic material to a polymeric matrix; and

placing the matrix into a chamber formed by a chamber body of a medical lead for elution of the genetic material to tissue of a patient at a stimulation site, wherein the genetic material is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site, the medical lead including a porous electrode, wherein the matrix elutes the genetic material to the stimulation site via the porous electrode.

Claim 36: The method of claim 35, further comprising:

blending extracellular collagen and gelatin; and

freeze-drying the blended extracellular collagen and gelatin to form the matrix.

Claim 37: The method of claim 35, further comprising:

identifying the genetic material and an elution rate; and

cross-linking the matrix based on the genetic material and the elution rate.

Claim 38: The method of claim 35, further comprising lyophilizing the matrix containing the genetic material.

Claim 39: The method of claim 35, further comprising:

freezing the chamber body containing the matrix and the genetic material; and

providing the frozen chamber body to a clinician,

wherein the clinician thaws the chamber body and assembles the lead to include the chamber body for implantation of the lead into the patient.

Claim 40: The method of claim 35, further comprising:

soaking the matrix in the genetic material; and

placing the matrix into the chamber.

Claim 41: The method of claim 40,

wherein soaking the matrix in the genetic material and placing the matrix into the chamber comprises soaking the matrix in the genetic material and placing the matrix into the chamber by a clinician, and

wherein the lead comprises a lead body, and the clinician assembles the lead body, chamber body and electrode prior to implantation of the lead within the patient.

Claim 42: The method of claim 35, wherein the chamber body is located at a distal end of the lead, the method further comprising immersing the distal end of the lead into the genetic material by a clinician to introduce the genetic material to the matrix.

Claim 46: The medical lead of claim 21, wherein the genetic material is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site and create a preferential conduction

pathway between the stimulation site and at least one of a bundle of His or a Purkinje fiber of a heart of the patient.

Claim 47: A medical lead comprising:

a lead body;

a porous electrode mounted on the lead body, wherein the porous electrode delivers electrical stimulation to a stimulation site within a patient;

a genetic material that causes expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site, wherein the expression of the at least one of the connexin or the gap-junction by the tissue at the stimulation site increases the conductivity of the tissue; and

a chamber body that defines a chamber containing a polymeric matrix that absorbs the genetic material and elutes the genetic material to tissue at the stimulation site via the porous electrode, wherein the polymeric matrix comprises extracellular collagen.

Claim 48: The medical lead of claim 47, wherein the matrix is cross-linked, and degrades to elute the absorbed genetic material at a degradation rate that is a function of the cross-linking.

Claim 49: The medical lead of claim 47, wherein the chamber body is separable from the lead for loading with the matrix and the genetic material.

Claim 50: The medical lead of claim 47, wherein the genetic material comprises at least one of a viral vector, a liposomal vector or plasmid deoxyribonucleic acid (DNA).

Claim 51: The medical lead of claim 47, wherein the genetic material is adapted to cause expression of connexin-43 by the tissue at the stimulation site.

Claim 52: The medical lead of claim 47, wherein the genetic material is adapted to cause expression of at least one of a metalloproteinase, an anti-inflammatory agent or an immunosuppressant agent.

Claim 53: The medical lead of claim 47, wherein the genetic material is adapted to cause expression of IκB.

Claim 54: The medical lead of claim 47, wherein the genetic material is adapted to cause expression of at least one of a connexin or a gap-junction by the tissue at the stimulation site to increase the conductivity of the tissue at the stimulation site and create a preferential conduction pathway between the stimulation site and at least one of a bundle of His or a Purkinje fiber of a heart of the patient.

APPENDIX B
EVIDENCE

None.

APPENDIX C

RELATED PROCEEDINGS

None.